REMARKS/ARGUMENTS

Claims 1-37 are currently pending in the above-identified application. Claims 10-37 have been withdrawn by the Examiner as drawn to a non-elected invention. Claim 8 is amended as set forth in detail herein. In addition, the specification is amended to place the "Related Applications" section as the first section of the application following the Title. No new matter is added. In light of the remarks and amendments set forth herein, Applicants respectfully request reconsideration of the instant application.

Restriction Requirement

The Examiner, contending that the present restriction requirement is proper, has made the requirement final. Applicants respectfully request reconsideration of the restriction requirement for the reasons set forth hereinbelow.

First, it is noted that the Examiner has maintained the restriction requirement on the basis of 37 C.F.R. § 1.475(b). As the Examiner is aware, this subsection of the C.F.R. states as follows:

> (b) An international or a national stage application containing claims to different categories of invention will be considered to have unity of invention if the claims are drawn only to one of the following combinations of categories:
>
> (1) A product and a process specially adapted for the manufacture of said product; or
>
> (2) A product and a process of use of said product; or
>
> (3) A product, a process specially adapted for the manufacture of the said product, and a use of the said product; or
>
> (4) A process and an apparatus or means specifically designed for carrying out the said process; or

> (5) A product, a process specially adapted for the manufacture of the said product, and an apparatus or means specifically designed for carrying out the said process.
>
> [37 C.F.R. § 1.475(b).]

As set forth further herein, the Examiner's position appears to rely exclusively on an interpretation of certain language in the above provision that is, at best, ambiguous. In fact, the Examiner's interpretation of § 1.475(b) (and application of this subsection to the present claims) is wholly inconsistent with the underlying standard for unity of invention, as well as inconsistent with other subsections of 37 C.F.R. § 1.475. Although Applicants pointed out some of these inconsistencies in Applicants' last response, the Examiner's reasoning for making the restriction requirement fails to reconcile or otherwise address these inconsistencies. Indeed, for the reasons below, the meaning of 37 C.F.R. § 1.475(b), when properly construed in light of the underlying standard for unity of invention and other provisions and guidelines set forth in the C.F.R. and MPEP, cannot be construed as requiring restriction of the present claims. Furthermore, the Examiner's assertions do ***not*** provide any reasons that would refute a fact that is essential to the determination of unity of invention, namely, that a $p27^{Kip1}$ polypeptide lacking a Cdk2 phosphorylation site (and gene encoding the polypeptide) is at least one "special technical feature" that is (a) common to claims 1-14 and 19-37; and (b) ***not*** disclosed or otherwise suggested by any prior art of record.

Under PCT Rule 13.2, the requirement for unity of invention among a group of inventions is fulfilled where the inventions share at least one special technical feature, *i.e.*, a technical feature defining "a contribution which each of the claimed inventions, where considered as a whole, makes over the prior art." MPEP § 1850 (citing PCT Rule 13.2). As indicated above, and previously noted in Applicants' response filed May 10, 2006, claims 1-14 and 19-37, constituting all claims of Groups I, II, and VII-X and part of Groups III-VI, recite a $p27^{Kip1}$ polypeptide lacking a Cdk2 phosphorylation site, or a gene encoding such a polypeptide. The only reference to which the Examiner has pointed as disclosing this feature is Nisar *et al.* (*Nature* 413:323-327, 2001), which is not prior art to the present invention as discussed further in Applicants' response to the rejection under 35 U.S.C. § 102. The Examiner has not pointed to

any other reference or other evidence showing that the mutant $p27^{Kip1}$ feature, as recited in the claims, is not novel and inventive over the prior art. For at least these reasons, the present restriction requirement is improper, at least as it has been applied to claims 1-14 and 19-37.

The Examiner, however, maintains that restriction is proper because 37 C.F.R. § 1.475(b) states that "[a]n international or a national stage application containing claims to different categories of invention will be considered to have unity of invention if the claims are drawn only to one of the following combinations of categories...." (Office Action at p. 2 (emphasis original).) The Examiner, therefore, appears to rely on the term "only," and interprets § 1.475(b) as permitting a finding of unity of invention only in the case where the claims of an application fit into one of the enumerated category combinations.

In response, Applicants first note that the language of 37 C.F.R. § 1.475(b) does not support the Examiner's position, at least insofar as the term "only" is not used to modify "if" (*i.e.*, to state "only if") and thus, by its terms, does ***not*** necessarily exclude ***other*** conditions in which unity of invention can be found. In other words, 37 C.F.R. § 1.475(b) is setting forth a guideline by which certain category combinations (each combination being drawn "only" to certain specified categories) will be found to have unity of invention *per se*, but is not setting forth a *per se* exclusionary rule to prohibit other category combinations that go beyond those enumerated.

The C.F.R. and MPEP are replete with other provisions and guidelines that support this latter interpretation of § 1.475(b) as a permissive rule, rather than an exclusionary one. For example, as previously noted in Applicants' response filed May 10, 2006, the section of the MPEP that specifically addresses category combinations specifically states that determining unity of invention under PCT Rule 13 "shall be construed as permitting, in particular, the inclusion [of certain category combinations]." MPEP § 1850 (III)(A) (emphasis provided). This section of the MPEP does not state anything regarding *per se* exclusion of certain category combinations.

Furthermore, the Examiner's interpretation of 37 C.F.R. § 1.475(b) as setting forth an exclusionary rule is wholly inconsistent with, ***inter alia***, subsection (c), which states as follows:

> (c) If an application contains claims to ***more*** or less than one of the combinations of categories of invention set forth in paragraph (b) of this section, unity of invention ***might*** not be present.

37 C.F.R. § 1.475(c) (emphasis provided). Because the term "might," as quoted above, clearly denotes only a possibility that unity of invention is not present, 37 C.F.R. § 1.475 clearly permits a finding of unity of invention in certain circumstances where the category combinations do not fit precisely into those enumerated in subsection (b). In particular, it is submitted that where an application is directed to more category combinations than those enumerated in subsection (b), whether there is unity of invention among the different categories must be determined according to the underlying unity of invention standard of a novel and inventive "special technical feature" as set forth in PCT Rule 13.2, rather than an overly rigid, restrictive, and inconsistent interpretation of the C.F.R. In this regard, the MPEP states the following:

> Although lack of unity of invention should certainly be raised in clear cases, it should neither be raised nor maintained on the basis of a narrow, literal or academic approach. There should be a broad, practical consideration of the degree of interdependence of the alternatives presented, in relation to the state of the art as revealed by the international search or, in accordance with PCT Article 33(6), by an additional document considered to be relevant. If the common matter of the independent claims is well known and the remaining subject matter of each claim differs from that of the others without there being any unifying novel inventive concept common to all, then clearly there is lack of unity of invention. If, on the other hand, there is a single general inventive concept that appears novel and involves inventive step, then there is unity of invention and an objection of lack of unity does not arise. For determining the action to be taken by the examiner between these two extremes, ***rigid rules cannot***

> ***be given*** and each case should be considered on its merits, ***the benefit of any doubt being given to the applicant***.
>
> [MPEP § 1850.]

In the present case, for reasons previously set forth, claims 1-14 and 19-37 share at least one "single general inventive concept" that is both novel and inventive over the art of record, to wit, a $p27^{Kip1}$ polypeptide lacking a Cdk2 phosphorylation site, or a gene encoding the polypeptide. Thus, a unity of invention issue should not arise at least with respect to these claims, and a rigid construction of 37 C.F.R. § 1.475(b), particularly a construction that is inconsistent with other guidelines and provisions for determining unity of invention, should not be used to maintain a restriction requirement against the pending claims.

Moreover, with respect to unity of invention as it relates to independent and dependent claims, the MPEP further states as follows:

> Unity of invention has to be considered in the first place only in relation to the independent claims in an international application and ***not*** the dependent claims....
>
> If the independent claims avoid the prior art and satisfy the requirement of unity of invention, no problem of lack of unity arises in respect of any claims that depend on the independent claims. In particular, it does not matter if a dependent claim itself contains a further invention....
>
> This method for determining whether unity of invention exists is intended to be applied even before the commencement of the international search. Where a search of the prior art is made, an initial determination of unity of invention, based on the assumption that the claims avoid the prior art, may be reconsidered on the basis of the results of the search of the prior art.
>
> [MPEP § 1850.]

In this case, Applicants note that, among claims 1-14 and 19-37, there are only 4 independent claims (claims 1, 10, 19, and 36). Each of these claims recite the special technical feature, "a mutant $p27^{Kip1}$ [gene/protein] lacking a Cdk2 phosphorylation site," which, for the

reasons already set forth, is novel and inventive over the cited art. Yet, in contravention of the clear guidelines quoted above, the Examiner maintains that three of these independent claims each forms the basis for more than one Group (*i.e.*, Groups I and II for claim 1, Groups III-VI for claim 10, and Groups VII-X for claim 19), and further maintains that there are ten separate Groups of invention among all the claims (independent and dependent) taken together. Consistent with MPEP § 1850, and for at least reasons already substantially set forth, there is unity of invention within and among independent claims 1, 10, 19, and 36, as well as any and all claims depending therefrom.

Applicants also believe it to be significant that no issue as to lack of unity of invention was raised by the International Searching Authority or the International Preliminary Examining Authority. (*See* International Search Report mailed July 2, 2004.) In this regard, the MPEP states as follows:

> ... it is clear that the decision with respect to unity of invention rests with the International Searching Authority or the International Preliminary Examining Authority. However, the International Searching Authority or the International Preliminary Examining Authority should not raise objection of lack of unity of invention merely because the inventions claimed are classified in separate classification groups or mearly for the purpose of restricting the international search to certain classification groups.
>
> [MPEP § 1850 (II).]

Here, the failure of the International Searching Authority or the International Preliminary Examining Authority to raise an issue of lack of unity with respect to the present claims is consistent with Applicants' interpretation (and, conversely, inconsistent with the Examiner's interpretation) of PCT Rules 13.1 and 13.2.

Accordingly, for the reasons above, reconsideration of the present restriction requirement is respectfully requested. There is unity of invention at least with respect to claims 1-14 and 19-37 and, therefore, the present restriction requirement, at least insofar as it has been

applied to these claims, is believed to be improper. The Examiner's interpretation of 37 C.F.R. § 1.475(b), as setting forth a rigid rule excluding any other category combinations than those enumerated, fails to take into account the principle, underlying standard by which unity of invention is determined, as well as other provisions and guidelines of the C.F.R. and MPEP. The result is that the Examiner has based her conclusion of alleged lack of unity on an interpretation of one provision of the C.F.R., such interpretation being inconsistent with other pertinent standards and guidelines. Applicants therefore respectfully request that the Examiner explain or otherwise reconcile the aforementioned inconsistencies in the Examiner's interpretation of 37 C.F.R. § 1.475(b). Applicant also respectfully requests that the Examiner show why the $p27^{Kip1}$ polypepetide or gene lacking a Cdk2 phosphorylation site is not a special technical feature that is both novel and inventive over the cited art and, thus, sufficient to impart unity of invention among claims 1-14 and 19-37. If the aforementioned inconsistencies cannot be adequately addressed, and if it cannot be shown why the recited mutant $p27^{Kip1}$ feature is not a special technical feature common to claims 1-14 and 19-37, then withdrawal of the restriction requirement as to these claims is again respectfully requested.

Group III and proposed rejoinder of claims limited to mouse

The Examiner has indicated that rejoinder of certain claims of Group III (claims 10-18) would be considered if these claims are limited to a transgenic mouse. Although Applicants presently decline to amend claims 10-18 to specify only mouse, Applicants appreciate the Examiner's indication of possible rejoinder of this subject matter.

Specification

The Examiner has objected to the specification, stating "the priority information should be listed in the first line of the specification." As noted above, the specification has been amended to place the "Related Applications" section as the first section following the Title, in

accordance with 37 C.F.R. § 1.77. In view of this amendment, withdrawal of the objection is respectfully requested.

Rejections Under 35 U.S.C. §112, first paragraph

Claims 1-9 stand rejected under 35 U.S.C. §112, first paragraph, as allegedly not enabled by the specification. The Examiner contends that the specification "does not reasonably provide for enablement for a non-mouse homozygous somatic cell or any non-mouse primordial germ cell, oocyte, egg, spermatocyte, sperm cell, fertilized egg, zygote or embryonic stem cell." (Office Action at p. 3.) According to the Examiner, the specification "fails to teach how to make any of these cells in vitro such that homologous recombination occurs resulting in these cell types having a gene-targeted insertion or replacement." The Examiner also states that "the only means known ... to obtain an oocyte or sperm cell comprising the claimed genetic alteration is by isolating it from a live animal," and that at the time of filing, "the only species for which a gene-targeting event can be passed on to a live animal is in mouse because gene-targeting has not been demonstrated in any totipotent cell, capable of giving rise to an animal, other than mouse ES cells." (*Id.*) The Examiner further contends that totipotent ES cells capable of giving rise to a germ-line transgenic animal were not available for any species other than mouse, and that the use of somatic cell nuclear transfer in making animals was "highly underdeveloped." (*Id.*, citing references.) With respect to homozygous somatic cells, the Examiner also alleges that homozygous gene-targeting events cannot be made in vitro. (*See id.*) This rejection is traversed for the reasons set forth below.

Initially, Applicants note that the specification need only disclose one method of making a claimed invention that bears a reasonable correlation with the entire scope of the claim in order to comply with the "how to make" requirement under 35 U.S.C. § 112, first paragraph. MPEP § 2164.01(b) (citing *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).) In addition, all that is necessary is that one skilled in the art "be able to practice the invention given the level of knowledge and skill in the art" (*id.* at § 2164.08), and thus the specification "need not disclose what is well known in the art" (*id.* (citing *In re Bucher*, 929 F.2d 660, 661, 18 USPQ2d

1331, 1332 (Fed. Cir. 1991))). Furthermore, the Federal Circuit has long recognized that, in determining whether undue experimentation would be necessary to practice an invention, "the key word is 'undue,' not 'experimentation.'" *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988). Accordingly, an extended period of experimentation "may not be undue if the skilled artisan is given sufficient direction or guidance." MPEP § 2164.06 (citing *In re Colianni*, 561 F.2d 220, 224, 195 USPQ 150, 153 (CCPA 1977)). The MPEP further states as follows:

> The test is not merely quantitative, since a ***considerable amount of experimentation is permissible***, if it is merely routine, or if the specification in question provides a reasonable mount of guidance with respect to the direction in which experimentation should proceed.
>
> [MPEP § 2164.06 (emphasis provided) (citing *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).]

In the present case, Applicants have described at least one method of making the recited transgenic cells that bears a reasonable correlation with the entire scope of the claims and that would not require experimentation regarded as undue to the skilled artisan seeking to carry out the claims. In particular, as noted by the Examiner, the specification describes the use of somatic cell nuclear transfer for making $p27^{Kip1}$ transgenic animals (from which $p27^{Kip1}$ transgenic cells can be obtained). (*See* specification at p. 27, l. 29, to p. 28, l. 18.) It is further noted that the Examiner appears to accept at least the fact that techniques for making transgenic animals by somatic cell nuclear transfer were known. It appears to be the Examiner's position however, that certain alleged difficulties in gene targeting to somatic cells render the process of somatic cell nuclear transfer as "unpredictable." As further set forth below, the skilled artisan would not regard any alleged difficulties in gene targeting as rendering somatic cell nuclear transfer as unpredictable, and any experimentation involved would not be considered by the skilled artisan as "undue."

First, with respect to Polejaeva and Campbell (*Theriogenology* 53:117-126, 2000; "Polejaeva"), the Examiner contends that this reference shows the "inefficiency and

unpredictability" of homologous recombination in somatic cells. (*See* Office Action at p. 6.) In particular, the Examiner states that Polejaeva teaches that "gene targeting in somatic cells is unpredictable because of the lower frequency of homologous recombination than ES cells, and a finite capacity for number of cell divisions." (*Id.*) Contrary to the Examiner's assertions, however, Polejaeva does not support "unpredictability" of gene targeting in somatic cells. Although frequencies of integration may be low, the frequencies of integration are known to the skilled artisan and are predictable. At the time of filing of the parent application, it was well established that integration of DNA in mammalian cells, including targeted homologous recombination, occurs at known or readily determinable frequencies. (*See, e.g.*, Capecchi, *Cell* 22:479-88, 1980 (attached hereto as Exhibit 1); Thomas and Capecchi, *Cell* 33:25-35, 1987 (attached hereto as Exhibit 2.) Therefore, the skilled artisan would recognize that structurally disrupting $p27^{Kip1}$ in somatic cells is not unpredictable but, rather, merely requires a predictable number of transfection and screening steps to identify cells having integrated transgene.

Thus, at most, gene targeting in somatic cells *in vitro* may be said to be relatively inefficient, involving a certain amount of experimentation to obtain a somatic cell having with the desired genetic modification. As set forth above, however, the quantity of any experimentation is not determinative, and even "a considerable amount of experimentation is permissible, if it is merely routine, or if the specification ... provides a reasonable mount of guidance with respect to the direction in which experimentation should proceed." *In re Wands*, 8 USPQ2d at 1404; MPEP § 2164.06. Here, because homologous recombination in somatic cells was known to occur at predictable frequencies, and because a certain amount of screening was expected in order to achieve and identify a desired integration event, gene targeting in somatic cells was indeed considered routine in the art.

Applicants also disagree with the Examiner's reliance on Thomson *et al.* (*Reprod. Supp.* 61:495-508, 2003) for the assertion that somatic cell nuclear transfer in making animals "was highly underdeveloped." (Office Action at p. 5, 2nd para.) The Examiner states the following in regard to Thomson *et al.*:

> Thomson *et al.* ... review the state of the art of gene targeting in somatic cells for use in nuclear transfer methodologies and state that procedures to enhance the lifespan of targeted somatic cells *in vitro* are needed. In particular, Thomson states that premature senescence often occurs, which makes in difficult to confirm a targeting event in somatic cells and that cloning efficiency has been negatively correlated with passage number....
>
> [Office Action at p. 5, last para. bridging to p. 6.]

In response, while Thomson suggests that certain modifications may improve somatic cell transfer procedures by overcoming premature senescence (*see, e.g.*, Thomson at p. 502, 1st & 2nd paragraphs), it is clear from Thomson that premature senescence, like homologous recombination, is primarily an issue of efficiency and does ***not*** preclude the ordinarily skilled artisan from achieving transgenic animals other than mouse using somatic cell nuclear transfer. Although Thomson suggests that premature senescence is an issue that should to be addressed in the future in order to "further" develop the nuclear transfer technology, Thomson nonetheless clearly acknowledges that the procedure of somatic cell nuclear transfer is a viable approach for achieving transgenic animals. Thomson states, for example, that "[i]n the short period since nuclear transfer was first performed, gene targeting in livestock has become a ***reality***." (Thomson at p. 495, Abstract (emphasis provided).) Furthermore, Polejaeva (also cited by the Examiner) states, *inter alia*, the following:

> The "ability to produce live offspring by nuclear transfer from cultured somatic cells provides a route for the precise genetic manipulation of large animal species. Such modifications include the addition, or "knock-in," and the removal or inactivation, "knock-out," of genes or their control sequences....
>
> [T]he development of somatic cell nuclear transfer has bypassed the need for livestock ES cells. Successful somatic cell nuclear transfer using an embryo-derived differentiated cell population was first demonstrated in sheep in 1996 .... Subsequently, the techniques was repeated and extended using cell populations derived from

> fetal and adult donors in sheep.... Furthermore, successful development has also been obtained in cattle ..., goats ... and mice.... [T]he primary significance of cloning is probably in the opportunities that this technology brings to the field of genetic manipulation.
>
> [Polejaeva and Campbell at p. 117 (Abstract and Introduction).]

Thus, the issue with premature senescence was not whether a gene targeting event and subsequent nuclear transfer could be predictably achieved. Rather, as stated by Thomson, the difficulty associated with premature senescence is the ability to "confirm the targeted event by Southern blot analysis before nuclear transfer." (*See id.* at p. 499, 2nd full para.) Irrespective of any difficulty with confirming the targeted event by Southern blot analysis, as indicated by Thomson, single-cell colonies can nevertheless be cloned by selection for resistance to an appropriate marker and used successfully for nuclear transfer. Even in the absence of gene targeting confirmation by Southern blot prior to nuclear transfer, nuclear transfer can be achieved and gene targeting confirmed *post hoc*. (*See id.* at p. 499.)

Consequently, as shown by Thomson and Polejaeva, although a certain quantity of single-cell clone screening and nuclear transfers were involved in achieving a gene targeting event in an animal, transgenic animals could predictably be produced by somatic cell nuclear transfer. The degree of screening and nuclear transfer needed to produce a given transgenic animal would not be considered as being any more than typically expected in the art, and therefore not undue. As previously noted, "the test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable mount of guidance with respect to the direction in which experimentation should proceed." MPEP § 2164.06 (citing *In re Wands*, 8 USPQ2d at 1404). In the present case, the specification provides more than a reasonable amount of guidance for producing transgenic animal having a cell as recited in claim 1. In particular, the specification teaches, *inter alia*, that a mutant $p27^{Kip1}$ protein lacking a Cdk2 phosphorylation site has a longer half-life in S phase than wildtype $p27^{Kip1}$ polypeptide. Further, as

acknowledged by the Examiner, the specification points to somatic cell nuclear transfer as a means for producing a mutant $p27^{Kip1}$ transgenic animal. As previously discussed, the skilled artisan would recognize that structurally disrupting $p27^{Kip1}$ in somatic cells is not unpredictable but, rather, merely requires a predictable number of transfection and screening steps to identify a targeted event. Consistent with this understanding in the art, Thomson teaches that somatic cell nuclear transfer had made gene targeting in non-mouse species a "reality." Accordingly, the skilled artisan would be able to produce a transgenic animal comprising the claimed transgenic cells without experimentation considered undue in the art.

With respect to the Examiner's assertions that the specification "has not contemplated a use for the claimed ... ES cells other than in making an animal," and that ES cells that exist and can be selected in culture "are not useful in making an animal with the exception of mouse ES cells," these assertions are directed to whether the recited ES cells have utility. In this regard, utility for a claimed composition is satisfied so long as there is at least one well-established or credible assertion of specific utility. *See* MPEP §§ 2107 (II) and 2107.02 (I). Here, irrespective of whether non-mouse ES cells are useful for making "whole animal" (germline) transgenics, the skilled artisan would readily accept that pluripotent non-mouse ES or ES-like cells are at least useful for making chimeric transgenic animals. Further, in view of Thomson *et al.*, the skilled artisan would readily recognize that non-mouse ES cells would also be useful for making transgenic animals as nuclear donor cells. In particular, Thomson suggests that ES cells from mouse or other species can be used as nuclear donor cells, for use in somatic cell nuclear transfer, because ES cells "retain a chromatin structure similar to that of cells in the early embryo and require less reprogramming." (Thomson at p. 502, 2nd para.) For at least these reasons, the recited ES cells are useful as of the effective filing date and therefore enabled for "how to use" under 35 U.S.C. § 112, first paragraph.

Applicants further disagree with the Examiner's remarks concerning homozygous somatic cells. The Examiner states that "homozygous gene targeting events cannot be made in vitro," and that an animal would "thus ... be necessary for homozygous somatic cells encompassed by the claims." (Office Action at p. 6, 2nd full para.) For reasons discussed above,

however, transgenic animals, including non-mouse transgenics, could be achieved by somatic cell nuclear transfer procedures without undue experimentation. The skilled artisan would readily recognize that such transgenic animals could be bred to homozygosity. Moreover, contrary to the Examiner's assertion that homozygous somatic cells "cannot be made in vitro," the skilled artisan would also readily understand that homozygous somatic cells can be made in vitro by using two rounds of gene targeting and screening.

Accordinlgy, for at least the reasons set forth above, the presently recited transgenic cells are enabled under 35 U.S.C. § 112, first paragraph. Withdrawal of the rejection is therefore respectfully requested.

Rejections Under 35 U.S.C. § 112, second paragraph

Claim 8 stands rejected under 35 U.S.C. §112, second paragraph, as allegedly indefinite, the Examiner asserting that is "unclear how a cell can be itself and its progeny at the same time.

While Applicants believe that the skilled artisan would understand the scope of claim 8 when read in light of the specification and therefore disagree with the rejection, claim 8 has been amended to further expedite prosecution of the instant application. Claim 8 now recites "[t]he transgenic cell of claim 1, comprising progeny of a second cell according to ~~the cell of~~ claim 1," thereby clarifying that the progeny and parental cells are different cells. In view of this amendment, withdrawal of the rejection is respectfully requested.

Rejections Under 35 U.S.C. §102

Claims 1-7 and 9 stand rejected under 35 U.S.C. §102(a) as allegedly anticipated by Malek *et al.* (*Nature* 413:323-327, 2001 (September 20); hereinafter "Malek").

Applicants traverse the instant rejection. Applicants submit herewith an *In re Katz* Declaration Under 37 C.F.R. § 1.132, which establishes that Malek describes the inventors' own work, as disclosed in priority application, USSN 60/352,391, filed January 28, 2002. Accordingly, Malek is not prior art under 35 U.S.C. § 102(a). Withdrawal of the rejection is respectfully requested.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 206-467-9600.

Respectfully submitted,

Date: December 21, 2006 By: Nicholas V. Sherbina

Nicholas V. Sherbina
Reg. No. 54,443

TOWNSEND and TOWNSEND and CREW LLP
Two Embarcadero Center, Eighth Floor
San Francisco, California 94111-3834
Tel: 206-467-9600
Fax: 415-576-0300
NVS:jms
60815909 v1